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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/679,147	10/05/2000	Tomoki Todo	066683/0188B	7711

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 01/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/679,147	TODO ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,15,16,19-21,23,48,49,55,58,60 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,15,16,20,21,23,48,49,55,58,60 and 62* is/are rejected.

7)☒ Claim(s) *19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's after-final amendment received on 10/29/04 has been entered. Claims 1, 7-9, 15-16, 19-21, 23, 48-49, 55, 58, 60, and 62 are currently pending in the instant application. In view of new grounds of rejection presented below, the finality of the previous office action is withdrawn and prosecution is re-opened. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Claim Rejections - 35 USC § 112

The rejection of claims 1, 7-9, 12-16, 19, 21, 23, 33, 35-37, 48-49, 52, 54, 59 and 61 under 35 U.S.C. 112, first paragraph, for scope of enablement, is withdrawn in view of applicant's cancellation or amendment of the claims.

The rejection of claims 8-9 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of applicant's amendments to the claims.

The indicated allowability of claims 55, 58, 60, and 62 is withdrawn in view of the newly discovered reference(s) to US Patent No. 6,051,428 (April 18, 2000). Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7-8, 15-16, 20-21, 23, 48-49, 55, 58, 60, and 62 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,051,428 (April 18, 2000), hereafter referred to as Fong et al., in view of Sturmhoefel et al. (October 1, 1999) Cancer Research, Vol. 59, 4964-4972. The applicant claims methods of activating or enhancing a T-cell response in a

patient with a tumor, comprising administering into a tumor a pharmaceutical composition comprising a herpes simplex virus vector comprising an expressible nucleotide sequence for a soluble costimulatory factor selected from B7-1-Ig and B7-2-Ig. The applicant further claims said methods wherein the method further comprises administering an additional nucleotide sequence for an immune modulator, and wherein the tumor is a hepatoma, melanoma, colon cancer cell, or breast cancer cell. In addition, the applicant claims said pharmaceutical compositions comprising a herpes simplex virus vector comprising an expressible nucleotide sequence for a soluble costimulatory factor selected from B7-1-Ig and B7-2-Ig.

Fong et al. teaches methods for inducing a protective immune response to tumor cells in a patient comprising transducing tumor cells by direct injection of the tumor in vivo with a replication defective herpes simplex virus amplicon vector comprising an costimulatory molecule necessary for the activation of T cells, wherein the costimulatory molecule is B7 (Fong et al., columns 29-30, claims 19, 21, and 29-30, column 3, lines 28-33, and 48-67, column 4, lines 1-10, and column 5-6, example 1). Fong et al. further teaches said methods wherein the tumor cells are transduced with more than one species of HSV amplicon encoding and expressing both a costimulatory molecule and a cytokine (Fong et al., column 30, claims 31-35). In addition, Fong et al., while generally teaching the treatment of tumors, specifically teaches the treatment of hepatomas, colorectal carcinomas, and lymphomas (Fong et al., column 30, claim 36, and columns 27-28, Tables 1-4).

Fong et al. differs from the instant invention by not specifically teaching that the costimulatory B7 molecule is a soluble B7 molecule such as B7-1-Ig or B7-2-Ig. Sturmhoefel et al. supplements Fong et al. by teaching vectors comprising soluble B7-1-Ig and B7-2-Ig , and

their use to produce soluble B7-1-Ig and B7-2-Ig to induce T cell mediated anti-tumor immunity against various types of tumors in vivo, including breast cancer, melanomas, sarcomas, and bladder carcinomas (Sturmhoefel et al., pages 4964-4965). Sturmhoefel et al. further provides specific motivation for using soluble B7-1-Ig or soluble B7-2-Ig over membrane bound B7 to treat tumors by demonstrating that soluble B7-1-Ig or soluble B7-2-Ig demonstrated increased tumor protection over membrane bound B7 (Sturmhoefel et al., page 4965, Table 1, and page 4966). Therefore, in view of advantages of treating tumors with soluble B7-1-Ig or soluble B7-2-Ig over membrane bound B7 as taught by Sturmhoefel et al., it would have been *prima facie* obvious to the skilled artisan to substitute the nucleotide sequence encoding soluble B7-1-Ig or soluble B7-2-Ig as taught by Sturmhoefel et al. for the membrane bound form of B7 in the pharmaceutical compositions comprising an HSV amplicon vector encoding and expressing an costimulatory molecule as taught by Fong et al. Further, in view of the efficacy in treating tumors with the recombinant HSV amplicons encoding a B7 molecule taught by Fong et al., and the increased tumor protection using soluble B7 over membrane bound B7 taught by Sturmhoefel et al., the skilled artisan would have had a reasonable expectation of success in using an HSV amplicon vector encoding soluble B7-1-Ig or soluble B7-2-Ig to treat tumors in a patient.

Claim 19 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,051,428 (April 18, 2000), hereafter referred to as Fong et al., in view of Sturmhoefel et al. (October 1, 1999) Cancer Research, Vol. 59, 4964-4972, as applied to claims 1, 7-8, 15-16, 20-21, 23, 48-49, 55, 58, 60, and 62 above, and further in view of U.S. Patent No. 6,764,675

(2004), hereafter referred to as Whitley et al. The applicant claims methods of activating or enhancing a T-cell response in a patient with a tumor, comprising administering into a tumor a pharmaceutical composition comprising a herpes simplex virus vector comprising an expressible nucleotide sequence for a soluble costimulatory factor selected from B7-1-Ig and B7-2-Ig, wherein the tumor is a brain tumor such as and astrocytoma, oligodendroglioma, meningioma, neurofibroma, or Schwannoma.

As discussed in detail above, Fong et al. in view of Sturmhoefel et al. provides teachings and motivation for making and using replication defective HSV vectors encoding soluble B7-1-Ig or soluble B7-2-Ig to treat tumors in a patient. While both Fong et al. and Sturmhoefel et al. teach the treatment of many types of tumors, neither reference specifically teaches the treatment of tumors such as meningiomas, glioblastomas or pituitary tumors. Whitley et al. supplements both Fong et al. and Sturmhoefel et al. by teaching that recombinant HSV vectors encoding immunomodulatory molecules are effective in treating brain tumors and tumors of the CNS, such as glioblastomas, meningiomas, and pituitary tumors (Whitley et al., column 4). Based on the teachings of Fong et al. and Sturmhoefel et al. that HSV vectors encoding costimulatory molecules can successfully treat various types of tumors, and the motivation provided by Whitley et al. for using HSV vectors to treat brain and CNS tumors, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use replication defective HSV vectors encoding soluble B7-1-Ig or soluble B7-2-Ig to treat brain or CNS tumors in a patient with a reasonable expectation of success.

Claim 9 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 9:30-6:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, **the new technology center fax number is (571) 273-8300**. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER